Pain and Anxiety

Deepak Kademani DMD MD FACS
Associate Professor, Oral and Maxillofacial Surgery
University of Minnesota

Introduction

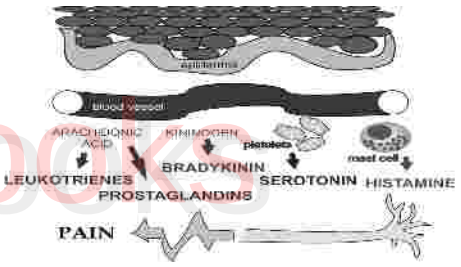
- 14 Lectures (Handbook of LA
- 2 Practical Sessions on LA and Nitrous
- LA April 10th 1-5pm (7th Flr, OMS)
- Nitrous May 28th 1-5pm (7th Flr, OMS)
- Midterm (60%) February 19th
- Final (40%) May 7th

Carl Koller 1884
First to use cocaine as a LA

Horace Wells

Ether Dome
MGH

Pain Pathways



The Ideal Local Anesthetic

- Water Soluble
- Non-irritating to Nerve
- Low Systemic Toxicity
- Short Induction Period
- Adequate Duration of Action
- No Side Effects
- Vasoconstriction Effect

Dental cartridge

Each cartridge is 1.8cc

Percent Solution

- Different anesthetics come in various concentrations
- These concentrations are given as a percentage
- .5% = 5 mg/cc
- 1% = 10 mg/cc
- 2% = 20 mg/cc

- *Multiply by 1.8cc to determine how many mg are in a dental cartridge*

Contents of a Dental Cartridge

- Anesthetic agent *eg: lidocaine, mepivicaine etc*
  - Anesthesia, vasodilation
- Vasoconstrictor: *epinephrine or levonordephrin*
  - Decreases absorption of anesthetic agent into blood, thereby increasing the duration of action and decreasing its toxicity

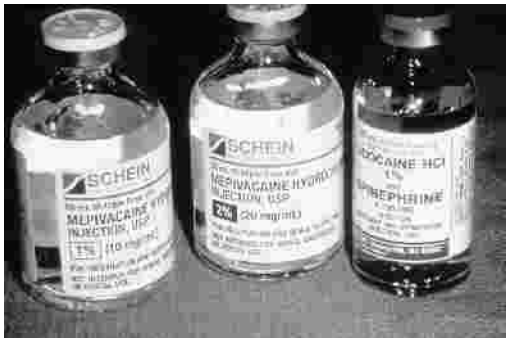
Contents cont:

- Sodium metabisulfite
  - Vasoconstrictor preservative
- Isotonic sodium chloride
- In multi-dose vials
  - Methylparaben may be present
    - Preservative for the anesthetic agent
    - Moderate incidence of allergic reaction
  - Not present in single-dose dental cartridges

Concentration of Vasoconstrictor

Concentration	Milligrams per milliliter
1:1000	1.0
1:2500	0.4
1:10,000	0.1
1:20,000	0.05
1:30,000	0.033
1:50,000	0.02
1:100,000	0.01
1:200,000	0.005

More common concentrations of vasoconstrictors In dental cartridges include:
1:50,000
1:100,000
1:200,000

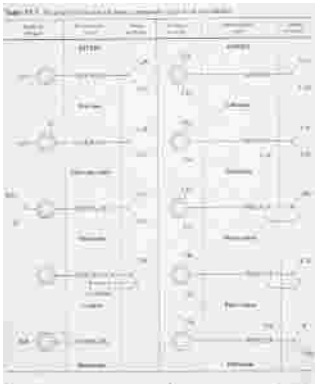


Chemical Configuration of LA

- Amides
- Esters

Locals are Comprised of:

- Aromatic lipophilic group
- Ester or amide linkage
- A hydrophilic secondary or tertiary amino group
- Water soluble when combined with acids



Amides vs Esters

- Major difference is method of metabolism
  - Amides: majority of the drug is metabolized in the liver
    - Use with caution in patients with severe liver disease
    - Use lower dose to avoid toxicity
  - Esters are metabolized in the plasma by pseudocholinesterase
    - PABA is a major metabolite of ester metabolism
      - Known allergen
    - Atypical pseudocholinesterase deficiency
      - Patients will not be able to metabolize; toxicity may ensue

Amide Local Anesthetics

- Articaine
- Bupivicaine
- Etidocaine
- Lidocaine
- Mepivacaine
- Prilocaine

Ester Local Anesthetics

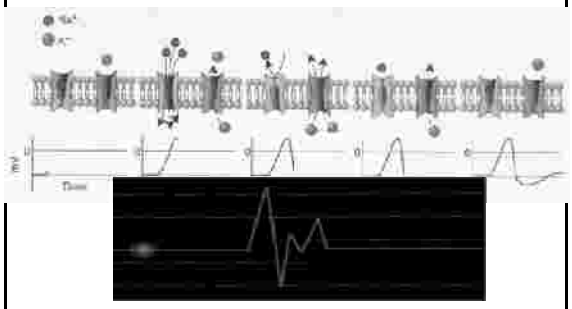
- Butacaine
- Cocaine
- Hexylcaine
- Piperocaine
- Tetracaine
- Benzocaine
- Chloroprocaine
- Procaine
- Propoxycaine

Pharmacology and Physiology

Nerve Conduction

- RMP -60 to -90
- Stimulus
- Slow Depolarization
- Threshold Reached
- Action Potential
- Repolarization

Formation of an Action Potential



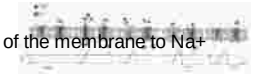
Nerve conduction

At resting potential

- Axoplasm is negative (around -70mV)
- Membrane is freely permeable to K^+ and Cl^-
- Membrane is only slightly permeable to Na^+

Nerve conduction

Nerve excitation causes



- Increase in the permeability of the membrane to Na^+
- The rapid influx of Na^+ to the interior of the nerve cell
- causes the axoplasm to become more positive
- The firing threshold is reached (-50 to -60mV)
- An action potential is created

Nerve conduction

Repolarization

- At the end of the action potential, the electric potential is positive (+40mV)
- The nerve membrane becomes impermeable to Na^+
- There is an efflux of K^+ and a return to normal resting potential

Mechanism of Action of LA Agents

Sodium channels are blocked preventing sodium ions from crossing the membrane

This causes blockage of the formation of an action potential

Mechanism of Action of LA Agents

- Depression of electrical depolarization
- Failure to achieve threshold potential level
- Lack of development of AP
- Conduction blockade

Clinical Characteristics of LA

- Onset
- Duration of Action
- Dosing

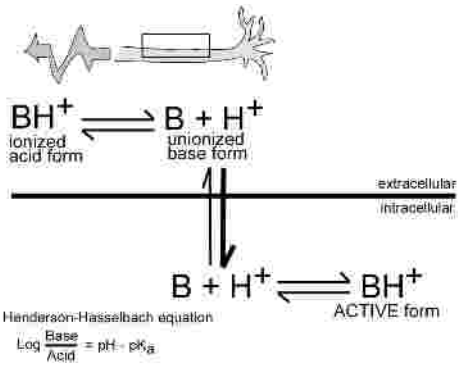
Henderson Hasselbach Equation

- Determines how much of a local anesthetic will be in a NI vs Ionized form
- Based on tissue pH and anesthetic Pk_a

Henderson Hasselbach

- Injectable local anesthetics are weak bases (pk_a=7.5-9.5)
- Part of the ionized form is converted to NI
- The NI base is what diffuses into the nerve
- The ionized form is responsible for action

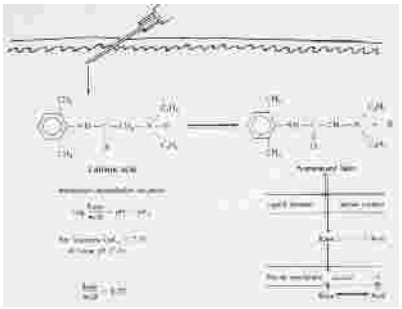
PHARMACOLOGY OF LOCAL ANESTHETICS



Henderson Hasselbach cont

Hence

- If the tissue is infected, the pH is lower (more acidic) and according to the HH equation; there will be less of the non-ionized form of the drug to cross into the nerve (rendering the LA less effective)
- Once some of the drug does cross; the pH in the nerve will be normal and therefore the LA re-equilibrates to both the ionized and nonionized forms; but there are fewer cations which may cause incomplete anesthesia



DISSOCIATION, PH AND PKA

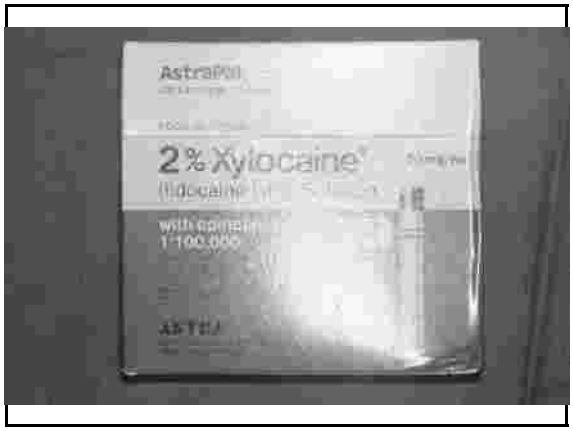
Listed below are the Pkas of commonly used local anesthetics:

Local Anesthetic	Ph = 7.4 (% uncharged)	Pka
Lidocaine	25	7.9
Mepivacaine	40	7.6
Prilocaine	25	7.9
Bupivacaine	18	8.1
Etidocaine	33	7.7
Procaine	2	9.1

Factors Affecting LA action

- Lower pK_a = more rapid *onset* (more LA in non-ionized form to diffuse through)
- Increased lipid solubility = increased *potency*
- Increased protein binding = longer *duration* of action

Maximum Recommended Doses of Local Anesthetics



Lidocaine HCL (Xylocaine)

- 2% concentration
  - Pulpal anesthesia 5 minutes
- Onset of action is 2-4 minutes
- Vasoconstrictor concentration
  - 1:100,000 epinephrine
  - 1:50,000 epinephrine
  - Pulpal anesthesia for 60-90 minutes

Mepivacaine HCL (Polocaine, Carbocaine)

- 3% concentration without vasoconstrictor
  - *Sulfite free*
  - Onset of action 30 sec - 4 min
  - Operating anesthesia time of 20-40 minutes
- 2% concentration with 1:20,000 levonordefrin
  - Operating anesthesia time of 1-5.5 hours

Long Acting LA

- 0.5% bupivicaine with 1:200,000 Epi
  - Marcaine
  - Max dose 1.3mg/kg; total max 90mg
  - Duration of action pulpal: 90-180 min, soft tissue: up to 12 hrs

Vasoconstrictors

Naturally Occurring Vasoconstrictors

- Epinephrine
- Norepinephrine

Adrenergic Agents

- Alpha: vasoconstriction
- Beta 1: cardiac smooth muscle
  - + chronotrope
  - + ionotrope
- Beta 2: bronchiolar smooth muscle
  - bronchodilation

Clinical Effects of Vasodilation

- Increase rate of absorption
  - Decreases duration of pain control
  - Increases anesthetic blood level
  - Increases potential for overdose

Vasoconstrictors should be used unless contraindicated

Mode of Action

- Attach to and directly stimulate adrenergic receptors
- Act indirectly by provoking the release of endogenous catecholamine from intraneuronal storage sites
- Combination of 1 and 2

Epinephrine (Adrenalin)

- Most potent vasoconstrictor used in dentistry
- Concentrations of 1:50,000 to 1:200,000 in dental cartridges

Concentrations of Vasoconstrictors

1:50,000	0.020mg/ml
1:100,000	0.010mg/ml
1:200,000	0.005 mg/ml

Calculation

1:50,000=

1gram/50,000ml=

1000mg/50,000ml=

1mg/50ml= 0.02mg/ml

Levonordefrin (Neo - Cobefrin)

- One fifth as active as epinephrine
- Acts on alpha sites

Vasoconstrictors - Unstable in Solution

Sodium metabisulfite added

Known allergen

Metabolism of Adrenergic Agonists

- Re-uptake
- Inactivation by catechol-o-methyltransferase COMT
- Monoamine oxidase MAO

Max dose of vasoconstrictors

- Healthy patient approximately *0.2mg*
- Patient with significant cardiovascular history: *0.04mg*
- How many carpules of 2% lidocaine with 1:100,000 epi is max dose for CV patient?

Max Dose for Vasoconstrictors (CV patient)

- 1 carpule = 1.8cc
- 1:100,000=.01mg/cc
- 0.01 X 1.8cc= 0.018mg
- 0.04/0.018=2.22 carpules

In a healthy adult patient

- *0.2/0.018=11.1 carpules*

Toxic Reactions and Side Effects

- Systemic toxicity
  - Inadvertent intravascular injection
  - Administration of large quantities
  - Altered drug metabolism
- Local tissue responses
- Idiosyncratic reactions
- Allergic reactions

Allergens in Local Anesthesia

- The agent itself
- PABA
- Sodium metabisulfite
- Methyl paraben

Systemic Toxicity of Local Anesthesia

- Convulsions
  - usually self limiting
  - can be treated with:
    - Diazepam
    - Barbiturate
    - Succinylcholine
- Respiratory depression
- Cardiovascular collapse

- *Principle 1*
- No drug ever exerts a single action

- *Principle 2*
- No clinically useful drug is entirely devoid of toxicity

- *Principle 3*
- The potential toxicity of a drug rests in the hands of the user

Thank You!